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In Vivo Trial Comparing Patients' Tolerance of Q-Switched Alexandrite (QS Alex) and Q-Switched Neodymium:Yttrium-Aluminum-Garnet (QS Nd:YAG) Lasers in the Treatment of Nevus of Ota

Henry H.L. Chan, MRCP,[1]* Walter W.K. King, FRSC,[2] Eric S.Y. Chan, MD,[2] Chun On Mok, FRCS,[2] Wai Sun Ho, FRCS,[2] Charlotte Van Krevel, MD,[1] and Lau WY, MD[2]

[1]Division of Dermatology, Department of Medicine and Therapeutics, Chinese University of Hong Kong, Shatin, Hong Kong, Republic of China
[2]Division of Plastic Surgery, Department of Surgery, Chinese University of Hong Kong, Shatin, Hong Kong, Republic of China

Background and Objectives: **Different types of Q-switched lasers have been found to be effective in the treatment of nevus of Ota. However, a clinical trial involving in vivo comparison of the use of different laser systems has not been performed. The aim of the present study was to compare the patient tolerance of Q-switched Alexandrite (QS Alex) and Q-switched neodymium:yttrium-aluminum-garnet (QS Nd:YAG) lasers in the treatment of nevus of Ota.**
Study Design/Materials and Methods: **Thirty-three patients (11 male, 22 female) were recruited for this study, and 45 treatment sessions were performed. Half of each lesion was treated with QS Alex and the other half with QS Nd:YAG laser. Patients were interviewed with a visual analog scale questionnaire immediately after treatment and 1 week later. Questions included the degree of pain, swelling, and bleeding.**
Results: **The immediate pain after treatment was more severe for QS Alex than for QS Nd:YAG laser. However, 1 week after laser therapy, most patients found QS Alex to be superior.**
Conclusion: **Patients tolerate QS-Alex better than QS Nd:YAG. This finding is important because patients with nevus of Ota are often children, and multiple laser sessions are necessary for complete resolution of the lesion. Lasers Surg. Med. 24:24–28, 1999.** **© 1999 Wiley-Liss, Inc.**

Key words: nevus of Ota; Q-switched lasers; tolerability

INTRODUCTION

Nevus of Ota is a condition characterized by benign dermal melanocytic proliferation. It affects approximately 0.2–0.6% of people of Asian extraction but is uncommon in Caucasians. Clinically it presents as bluish hyperpigmentation along the first or second branches of the trigeminal nerve. Previous treatment modalities such as surgical excision or dermabrasion were ineffective and were associated with a significant risk of scarring. Different types of Q-switched lasers have been found to be effective in the treatment of nevus of Ota, including Q-switched ruby [1], Q-switched Alexandrite (QS Alex) [2], and Q-

*Correspondence to: Dr. Henry H.L. Chan, Division of Dermatology, Department of Medicine and Therapeutics, 9th Floor Clinical Science Building, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong, Republic of China. E-mail: henrychan@cuhk.edu.hk

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TABLE 1. Demographic Data and Patient Characteristics

	No. of patients
Onset age (years)	
At birth	10
<1	6
1–6	7
>6	8
Precipitating factor	
Trauma	2
Puberty	1
Sunshine	3
Unknown	16
Size of lesion (mean surface area, cm^2)	
<30	17
30–60	12
>60	5
Side of lesion	
Left	17
Right	15
No. of laser sessions attended	
3	9
2	28
1	5

switched neodymium:yttrium-aluminum-garnet (QS Nd:YAG) [3] lasers. Multiple treatment sessions are necessary to achieve significant or even complete lightening. As a result, patient acceptability to complications such as pain and swelling that commonly occur after laser treatment is important. The aim of the present study was to compare the patients' tolerance of QS Alex and QS Nd:YAG lasers in the treatment of nevus of Ota.

PATIENTS AND METHODS

Thirty-two patients (10 male, 31%; 22 female, 69%; age range = 6–63 years) with nevus of Ota were recruited from the Dermatology Clinic of the Prince of Wales Hospital, Hong Kong. Forty-two treatment sessions were performed on these patients (Table 1). Although only 32% of these patients had the lesion at birth, most developed it before they were 1 year old (51%). Precipitating factors could be identified in only six cases (19%). The Ethical Committee of the Chinese University of Hong Kong approved the study, and all patients signed written consent forms before entering the trial. Before treatment, the research nurse used an ink pen to divide each lesion into two halves and took clinical photographs. Half of each lesion was treated with QS Nd:YAG 1,064-nm laser (Medlite Q-switched Nd:YAG laser system; Continuum Biomedical, Inc.) by using a 2-mm spot size, 10-Hz repeat rate, and pulse duration of 6 nsec. The fluences ranged from 7 to 9 J/cm^2 (average fluence = 7.2 J/cm^2) and were determined by the clinical response defined as whitening immediately after laser therapy. The other half was treated with QS Alex laser (MedAlex Q-switched Alexandrite laser system; Continuum Biomedical, Inc.) by using a spot size of 2 mm, 8-Hz repeat rate, and pulse duration of 75 nsec. Fluences ranging from 6 to 9 J/cm^2 (average fluence = 7.1 J/cm^2) were used, and immediate whitening was used as the clinical endpoint. The same operator (H.H.L.C) provided all treatments. In all cases, EMLA cream (Astra, Sweden) was applied to the lesion 2 hr before treatment and tegaderm (3M Health Care, Germany) was used to occlude the area. EMLA was removed immediately before laser surgery by the use of wet gauze. Lead eyeshields were inserted after instillation of lignocaine eye drops as protection during laser therapy. After treatment, patients were advised to clean the laser-treated area with mild soap and water twice daily. Bactroban cream (Beecham Pharmaceutical, England) was applied to the area twice a day.

A week after treatment, patients were requested to return for wound assessment. A research nurse interviewed the patients regarding their experiences (such as pain during and after treatment) immediately after treatment and a week afterward. The questionnaire consisted of questions about the degree of pain, swelling, discomfort, lightening, and bleeding. Pain was defined as a painful sensation that warranted the use of an oral analgesic; discomfort was defined as an uncomfortable feeling for which an analgesic was not necessary. The patients were also asked which laser was their preferred choice of treatment. Next to each question was a horizontal line measuring 10 cm, marked by number 0 on one side and number 10 on the other side. Patients were informed that 0 was the minimum and 10 was the maximum and were asked to mark accordingly. During the follow-up visit, they were allowed to look at their previous scores and answer the questionnaire at the same time. Additional questions about such matters as disruptions of sleep and work were also asked. The scores were analyzed with Student's *t* test.

RESULTS

Symptoms After Laser Therapy

The immediate pain after laser therapy was more severe for QS Alex than for QS Nd:YAG.

TABLE 2. Symptoms After Laser Therapy: Comparison of the Two Systems

Laser system	Immediate pain score[a]	1 Week pain score	1 Week discomfort score[a]	1 Week swelling score	1 Week wound score	1 Week lightening score
Alexrandrite	5.52*	2.13*	2.26**	1.12**	0.55*	1.68
Nd:YAG	4.35	3.18	3.58	2.39	1.05	2.09

*$P < 0.05$.
**$P < 0.01$.
[a]Pain is defined as a painful sensation that warrants the use of an oral analgesic; discomfort is defined as an uncomfortable feeling for which an analgesic is not necessary.

However, 1 week after laser therapy, most patients found QS Alex to be superior to QS Nd:YAG in terms of pain, discomfort, swelling, and degree of wound (Table 2). Overall, 54% of the patients preferred QS Alex to QS Nd:YAG as a treatment modality.

Work, Social Activity, and Sleep

Thirty-one percent of the patients felt that their work or study was affected by the laser treatment, and 49% felt that their social activities were affected. Sleep disturbances were noticed by 24% of patients (Table 3).

TABLE 3. Disruption of Daily Life After Laser Therapy

	% Patients
Affect work/study	
Yes	31
No	69
Affect social activities	
Yes	49
No	51
Affect sleeping	
Yes	24
No	76

DISCUSSION

Nevus of Ota was named after a Japanese dermatologist who first described the lesion in 1939 [4]. It is common in the Asian community and affects up to 0.5% of the population. Our findings confirm the observations by Hidano et al. [5] who showed that, of 240 patients with nevus of Ota, there was a female predominance, with a male:female ratio of 1:4.8. Furthermore, 52% of their patients noted the lesions after 1 year of age and 41% after 11 years of age. Such data suggest that there are two peaks of onset for nevus of Ota, one at birth and the other at around puberty. This does not imply that those with a late onset have an acquired lesion. Because nevus of Ota is widely regarded as a form of dermal melanocytic hamartoma, all patients would have the nevus at birth. Some lesions, however, do not become clinically apparent until later on in life, when a triggering factor stimulates the production of melanin from existing nevoid melanocytes. It has been suggested that female sex hormones are a potent stimulus, and this suggestion is supported by the female predominance, by the frequent onset during puberty, and by the reported color variation seen in menopause [6]. Indeed, female sex hormones have an important role in the development of other melanocytic conditions such as melasma. Other stimuli such as trauma or ultraviolet light exposure have also been documented [5,7] to trigger the onset of the nevus.

Because the condition occurs in the face, cosmetic disfiguration is inevitable. Previous treatment modalities such as surgical excision, cryotherapy, and dermabrasion have been ineffective and have been associated with a significant degree of scarring. Continuous-wave argon laser has been used with some success [8]. Although the wavelength of the laser matches the absorption spectrum of melanin, heat dissipation to the surrounding tissue implies that scarring can result. The theory of selective photothermolysis has revolutionized the use of laser as a treatment modality [9]. Q-switched lasers are lasers that generate high-energy radiation with a very short pulse duration (in terms of nanoseconds). Such devices produce intense energy that lead to a rapid rise in temperature (1,000°C) within the target subcellular chromophore. Because the laser pulse duration is shorter than the thermal relaxation time of the target, a temperature gradient is created between the target and its surrounding tissue [9–12]. When such a temperature gradient collapses, it generates localized shockwaves, causing fragmentation of its targets [9,12,13]. This form of photomechanical reaction is thought to be responsible for the melanosomal disruption seen after Q-switched laser irradiation for nevus of Ota [1,9,14–16]. Apart from the photomechanical re-

action, the photothermal effect is also important. Previous studies have indicated that the threshold response in the treatment of pigmented lesions by Q-switched laser is a transient, immediate, ash-white discoloration [13]. Immediate whitening correlates with the formation of steam pockets around the melanocytes, which occur as a result of localized water evaporation [17,18]. As a result, most studies now use immediate whitening as a clinical endpoint [1,2,18] for the treatment of nevus of Ota.

Q-switched ruby (694 nm) laser was the first Q-switched laser shown to be effective in the treatment of nevus of Ota [1]. Multiple treatment sessions (≥4) are necessary to achieve an excellent response (≥70% lightening). Other lasers have since been developed and these include QS Nd:YAG (1,064 nm) and QS Alex (755 nm) lasers [2,3]. With a longer wavelength, they have a greater depth of penetration and therefore carry a significant advantage in the treatment of dermal melanosis as seen in nevus of Ota. Another important factor is the absorption spectrum of melanin. Anderson and Parish [19] pointed out that, although the absorption spectrum of melanin is 250–1,200 nm, the absorption increased gradually over the shorter wavelength. In fact, absorption by melanin over 1,100 nm is negligible. Therefore, QS Nd:YAG laser is less well absorbed by melanin than is QS Alex. Previous studies have shown that the energy used for QS Nd:YAG laser to produce a clinical response is significantly higher than that used for QS Alex [2,3].

Although both QS Nd:YAG and QS Alex lasers have been found to be effective in the treatment of nevus of Ota, clinical trials comparing the two systems have not been performed. Because most patients develop the lesions before the age of 6 years, there is now a tendency to perform treatment early in life with the aim of avoiding psychological trauma. Furthermore, for the lesion to be completely resolved, multiple treatment sessions are required. Patients' acceptability to laser therapy is therefore important. Our study is the first in vivo trial looking at the patients' tolerance of the two systems. An in vivo study is particularly useful in the assessment of symptoms such as pain and swelling. Our findings indicated that, although QS Alex laser caused more immediate pain, patients tolerate it better than QS Nd:YAG laser a week after therapy. Our data correlate with the clinical observations. Immediately after treatment with QS Alex laser, tissue swelling occurs, which correlates with the degree of immediate pain. In the case of QS Nd:YAG laser, tissue and blood splatterings are the more predominate features. Because tissue healing takes time, QS Nd:YAG laser is associated with a greater degree of symptomatic discomfort a week after laser surgery.

By inducing different types of tissue–laser interaction, the clinical endpoints are different. Although a pigment such as melanin is the main target chromophore for all the Q-switched lasers used in the treatment of nevus of Ota, the near infrared wavelength (1064 nm) of QS Nd:YAG laser also means that it is weakly absorbed by water. This would explain why tissue and blood splattering commonly occur with the use of QS Nd:YAG laser. In fact, Goldberg and Whitworth used QS Nd:YAG laser as a resurfacing laser [20].

In contrast to the previous findings [2,3] that showed that higher energy was required for QS Nd:YAG laser to provide a clinical response, there were no significant differences between the energy levels we used for the two systems. This result may be due to operator bias, a drawback of the study design. Because the clinical endpoint is defined by subjective assessment, the operator could have the tendency to use similar energy levels, which could lead to using too low energy for QS Nd:YAG laser and too high energy for QS Alex laser. If symptomatic discomfort is related to the energy level, then our results would be an underestimation of the symptomatic discomfort induced by the use of QS Nd:YAG laser and an overestimation of that incurred by QS Alex laser. Despite such a pitfall, the result clearly is more favorable to QS Alex laser. Indeed, QS Alex laser is the overall preferred type of treatment.

In conclusion, with regard to pain, discomfort, swelling, and wound healing, QS Alex laser is more acceptable to patients with nevus of Ota as a treatment modality than is QS Nd:YAG. A long-term study is necessary to examine the long-term complications and clinical efficacy of the two systems.

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